

## REMARKS

Reconsideration of this application, as amended, is respectfully requested. The Applicants draw the Examiner's attention to the Applicants' related co-pending applications and issued patents (see Appendix A) directed to nanoparticles and methods of preparation and use thereof. Office actions have already issued in most of these cases. In particular, the Applicant wishes to draw the Examiner's attention to the allowed claims (copy attached) for U.S. serial no. 09/967,409 (Atty case no. 00-713-i6).

The Applicants note that the Examiner did not return executed copies of the PTO 1449 form for the 6<sup>th</sup> Supplemental IDS that was hand delivered to the Examiner on September 9, 2002. The Applicants request that the Examiner fully execute the PTO 1449 form for the 6<sup>th</sup> Supplemental IDS and return a copy of the executed PTO 1449 form to the undersigned representative. A copy of the 6<sup>th</sup> Supplemental IDS, associated PTO 1449 form, and PTO stamped postcard acknowledging receipt of the IDS, PTO 1449 form and references are attached. The Examiner is requested to contact the undersigned representative if the Examiner would like to have another copy of the references.

Claims 2-24, 29-32, 42, 43, and 106-121 were previously pending in this application. Claims 106 and 121 were cancelled and claims 42 and 113 were amended to further clarify the invention. Support for the amendment of claims 42 and 113 can be found in the presently cancelled claims. Accordingly, no new matter has been added to this application as a result of the present amendment. Claims 2-24, 29-32, 42, 43, and 107-120 are now pending in this application.

Turning now to the Office action, the Applicants note, with thanks, that the Examiner has found claims 2-24 and 29-32 to be allowable. The Examiner, however, rejected claims 42, 43 and 107-119 under 35 U.S.C. section 103(a) as being unpatentable over Yguerabide et al. (U.S. Patent No. 6,214,560)("Yguerabide") in view of Nelson (U.S. Patent No. 5,942,610)("Nelson"). The Examiner alleged that it would have been obvious to employ fluorophore labels as taught by Nelson in Yguerabide's method for detection target analytes and thus arrive with the Applicant's claimed invention. The Applicants respectfully traverse this rejection.

The Federal Circuit reiterated the manner in which obviousness rejections are to be reviewed. Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, "a proper analysis under § 103 requires, *inter alia*,

consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success." *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 4631), citing *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 U.S.P.Q. 2d 1529, 1531 (Fed. Cir. 4628). As the Federal Circuit emphasized by succinctly summarizing: "Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the Applicants' disclosure." *Id.* Contrary to the Examiner's position, neither Yguerabide nor Nelson, alone or in combination, suggest doing what the Applicants have done.

Specifically, the Examiner alleged that Yguerabide taught detection and measurement of one or more analytes in a sample using particles of specific composition and size using light scattering. The discussion is found starting in col. 82, line 35, of Yguerabide. Col. 83 provides further discussion regarding particle size and particle binding to a surface. Nelson is remote to the invention and merely describes methods for attaching labels to oligonucleotides. There is no suggestion or disclosure of any method in Yguerabide or Nelson that employs metal or semiconductor nanoparticle detection probes wherein "in the presence of the nucleic acid target and under hybridization conditions, the nanoparticles having oligonucleotides bound thereto form a complex with the nucleic acid target, the resulting complex having a sharp melting profile and increased melting temperature relative to a comparable complex without nanoparticles, to allow for selective discrimination of any nucleotide insertion, deletion, or mismatch in the nucleic acid target." See claims 42 and 113. Methods that employ such nanoparticle-oligonucleotide conjugates exhibit melting (dehybridization) profiles that are extremely narrow compared to the profiles obtained using the same oligonucleotides not attached to nanoparticles, and extraordinary selectivity (detection as little as a single base difference) and sensitivity (detecting as little as 10 femtomoles of nucleic acid without amplification) have been obtained using these conjugates in such assays (see particularly Examples 5, 7 and 19) of the application. Claims 42, 43 and 107-120 thus recite limitations that are neither taught, made obvious, or suggested by the cited references. Thus, the Applicant respectfully submits that the combination of Yguerabide and Nelson cannot be applied to support a section 103(a) rejection of the aforementioned claims.

In conclusion, the Applicants respectfully submit that the claims in this application are in allowable condition and request a Notice to this effect.

Reconsideration of this application is respectfully requested and a favorable determination is earnestly solicited. The Examiner is invited to contact the undersigned representative if the Examiner believes that this would be helpful in expediting the prosecution of this application.

Respectfully submitted,

Date:

12/11/03



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Page 1 of 6

**APPENDIX A**

<b>ATTY Case No.</b>	<b>Serial No./ Filing Date</b>	<b>Inventors/Title</b>	<b>Status</b>
<b>00-653-A</b>	U.S. 09/927,777 Filed 8/10/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton, Garamella, Li, Park/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERETO AND USES THEREFORE	ALLOWED
<b>00-713-B1</b>	09/923,625 Filed 8/7/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERETO AND USES THEREFOR	PENDING
<b>00-713-C</b>	09/344,667, filed 6/25/99	Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERETO AND USES THEREFORE	U.S. Patent No. 6,361,944, issued 3/26/02
<b>00-713-I</b>	U.S.S.N 09/603,830 Filed 6/26/00	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton; NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERETO AND USES THEREFOR	U.S. Patent No. 6,506,564, issued 1/14/03
<b>00-713-I-1</b>	09/961,949 9/20/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton;	U.S. Patent No. 6,582,921, issued June 24, 2003

<b>ATTY Case No.</b>	<b>Serial No./ Filing Date</b>	<b>Inventors/Title</b>	<b>Status</b>
		NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERE TO AND USES THEREFOR	
<b>00-713-I-2</b>	09/957,318 9/20/01	See 00-713-I-1	ALLOWED
<b>00-713-I-3</b>	09/957,313 9/20/01	See 00-713-I-1	U.S. Patent No. 6,645,721, issued 11/11/03
<b>00-713-I-4</b>	09/966,491 9/28/01	See 00-713-I-1	U.S. Patent No. 6,610,491
<b>00-713-I-5</b>	09/966,312 9/28/01	See 00-713-I-1	ALLOWED
<b>00-713-I-6</b>	09/967,409 9/28/01	See 00-713-I-1	ALLOWED
<b>00-713-I-7</b>	09/974,500 10/10/01	See 00-713-I-1	ALLOWED
<b>00-713-I-8</b>	09/974,007 10/10/01	See 00-713-I-1	PENDING
<b>00-713-I-9</b>	09/973,638 10/10/01	See 00-713-I-1	PENDING
<b>00-713-I-10</b>	09/973,788 10/10/01	See 00-713-I-1	ALLOWED
<b>00-713-I-11</b>	09/975,062 10/11/01	See 00-713-I-1	ALLOWED
<b>00-713-I-12</b>	09/975,376 10/11/01	See 00-713-I-1	PENDING
<b>00-713-I-13</b>	09/975,384 10/11/01	See 00-713-I-1	PENDING
<b>00-713-I-</b>	09/975,498	See 00-713-I-1	ALLOWED

<b>ATTY Case No.</b>	<b>Serial No./ Filing Date</b>	<b>Inventors/Title</b>	<b>Status</b>
<b>14</b>	10/11/01		
<b>00-713-I- 15</b>	09/975,059 11/11/01	See 00-713-I-1	PENDING
<b>00-713-I- 16</b>	09/976,601 10/12/01	See 00-713-I-1	PENDING
<b>00-713-I- 17</b>	09/976,968 10/12/01	See 00-713-I-1	PENDING
<b>00-713-I- 18</b>	09/976,971 10/12/01	See 00-713-I-1	ALLOWED
<b>00-713-I- 19</b>	09/976,863 10/12/01	See 00-713-I-1	PENDING
<b>00-713-I- 20</b>	09/976,577 10/12/01	See 00-713-I-1	ALLOWED
<b>00-713-I- 21</b>	09/976,618 10/12/01	See 00-713-I-1	PENDING
<b>00-713-I- 22</b>	09/981,344 10/15/01	See 00-713-I-1	ALLOWED
<b>00-713-I- 23</b>	09/976,900 10/12/01	See 00-713-I-1	PENDING
<b>00-713-I- 24</b>	09/976,617 10/12/01	See 00-713-I-1	ALLOWED
<b>00-713-I- 25</b>	09/976,378 10/12/01	See 00-713-I-1	PENDING
<b>00-713-i- 26</b>	10/410,324 04/10/03	See 00-713-I-1	PENDING
<b>00-713-L</b>	U.S.S.N. 09/693,005 Filed 10/20/00	Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED	U.S. Patent No. 6,495,324, issued 12/17/02

<b>ATTY Case No.</b>	<b>Serial No./ Filing Date</b>	<b>Inventors/Title</b>	<b>Status</b>
		THERETO AND USES THEREFORE	
<b>00-713-M</b>	U.S.S.N. 09/693,352 Filed 10/20/00	Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERETO AND USES THEREFORE	U.S. Patent No. 6,417,340, issued 7/9/02
<b>00-714-G</b>	U.S. 09/830,620 Filed 8/15/01	Mirkin, Nguyen/ NANOPARTICLES WITH POLYMER SHELLS	PENDING
<b>00-715-A</b>	U.S. 09/760,500 Filed 1/12/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton; Garamella, Li/ METHOD OF ATTACHING OLIGONUCLEOTI DES TO NANOPARTICLES AND PRODUCTS PRODUCED THEREBY	ALLOWED
<b>00-1085-A</b>	U.S.S.N. 09/820,279 Filed 3/28/01	Mirkin, Letsinger, etc./ METHOD AND MATERIALS FOR ASSAYING BIOLOGICAL MATERIALS	ALLOWED
<b>00-1086-A</b>	U.S. 09/903,461 Filed 7/11/01	Letsinger, Garimella/ METHOD OF DETECTION BY ENHANCEMENT OF SILVER STAINING	U.S. Patent No. 6,602,669, Filed 8/5/03
<b>01-565-A</b>	USSN 10/125,194 Filed 4/18/02	Mirkin, Nguyen, Watson, Park/ OLIGONUCLEOTI DE-MODIFIED ROMP POLYMERS	PENDING

<b>ATTY Case No.</b>	<b>Serial No./ Filing Date</b>	<b>Inventors/Title</b>	<b>Status</b>
		AND CO- POLYMERS	
<b>01-599-A</b>	U.S.S.N. 10/291,291 Filed 11/08/02	Storhoff/NOVEL THIOL-BASED METHOD FOR ATTACHING OLIGONUCLEOTI DES TO NANOPARTICLES	PENDING
<b>01-661-A</b>	U.S.S.N. 10/034,451 Filed 12/28/01	Mirkin, Cao, Jin/ DNA-MODIFIED CORE-SHELL AG/AU NANOCRYSTALS	PENDING
<b>01-661-C</b>	U.S.S.N. 10/153,483 Filed 5/22/02	Mirkin, Cao, Jin/ DNA-MODIFIED CORE-SHELL AG/AU NANOCRYSTALS	PENDING
<b>01-661-E</b>	U.S.S.N. 10/397,579 3/26/03	Mirkin, Cao, Jin/ DNA-MODIFIED CORE-SHELL AG/AU NANOCRYSTALS	PENDING
<b>01-1565-A</b>	U.S.S.N. 10/266,983 Filed 10/08/02	Park, Taton, Mirkin/ARRAY- BASED ELECTRICAL DETECTION OF DNA USING NANOPARTICLE PROBES	PENDING
<b>01-1705-A</b>	U.S.S.N. 10/108,211 Filed 3/27/02	Nam, Park, Mirkin/BIO- BARCODES BASED ON OLIGONUCLEOTI DE-MODIFIED NANOPARTICLES	PENDING
<b>02-338-B</b>	USSN 10/172,428 Filed 6/14/02	Cao, Jin, Nam, Mirkin/MULTIHA NNEL DETECTION USING NANOPARTICLE	PENDING



ATTY Case No.	Serial No./ Filing Date	Inventors/Title	Status
		PROBES WITH RAMAN SPECTROSCOPIC FINGERPRINTS	
02-338-C	10/431,341 5/7/03	Cao, Jin, Nam, Mirkin/MULTI- CHANNEL DETECTION USING NANOPARTICLE PROBES WITH RAMAN SPECTROSCOPIC FINGERPRINTS	PENDING